Breast cancer patients with a spectrum of recurrence risks may potentially be candidates for thermal ablation of their tumor. Initial pivotal trials perhaps may enroll patients with early disease and a low risk for recurrence. Oftentimes, when a device is demonstrated as safe and effective in one population, efforts are made to expand the use of the technology to a broader population of patients. Therefore for each of the following questions, please make recommendations specifying the classification of patients and discuss under which circumstances repeat initial studies of minimally invasive ablation followed by open resection should again be undertaken prior to extrapolating the results to a broader patient group.

Questions

1. Please discuss the level of evidence that would be required in initial studies that treat the primary breast cancer by minimally invasive ablation followed by immediate lumpectomy for pathologic examination of margins (i.e. ablate and resect studies), to permit initiation of studies that use minimally invasive ablation to definitively treat the cancer without follow-up resection (i.e., ablate and follow studies). Include in your discussion the appropriate level of evidence (confidence level) required to characterize the following:
    a) Accuracy of the device to target the specific lesion
    b) Completeness of ablation (including size of tumor free margins)
    c) Reproducibility among different investigators
    d) Reproducibility among different centers

2. Please discuss the type of pivotal study that would need to be performed in order to demonstrate the efficacy of a thermal ablation device to provide local breast cancer treatment in lieu of lumpectomy. Please address the appropriate:
    a) Patient population with respect to primary tumor size, nodal status, histology, mammographic findings, ultrasound findings, biological markers, age, etc.
    b) Control group
    c) Assessments (e.g. radiographic modalities, biopsy, etc.) and the frequency of these assessments.
    d) Duration of follow-up to demonstrate efficacy of treatment (in lieu of lumpectomy)

3. Radiation therapy and chemotherapy may be concomitantly used to treat breast cancer patients who may receive thermal ablation of their tumor in lieu of lumpectomy. One concern is that thermal ablation of the cancer may affect the surrounding breast tissue radio/chemosensitivity. Please provide recommendations regarding the best way that this concern may be addressed in clinical trials aimed at understanding the safety and effectiveness of thermal ablation for the treatment of breast cancer.

4. Neoadjuvant and adjuvant chemotherapy or radiation therapy may affect the ability to radiographically visualize the margins of breast cancers either at the

time of minimally invasive treatment or at follow-up for tumor recurrence. Please discuss how limitations of radiographic visualization will affect the selection of candidates for these procedures, and the appropriate follow-up for these patients.